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## hESC Differentiation toward an Autonomic Neuronal Cell Fate Depends on Distinct Cues from the Co-Patterning Vasculature.

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### Public Summary:

urovascular co-patterning at the earliest stages of human embryogenesis, we developed a human embryonic stem cell model to mimic the developing epiblast. Contact of ectoderm-derived neural cells with mesoderm-derived vasculature is initiated via the neural crest (NC), not the neural tube (NT). Neurovascular co-patterning then ensues with specification of NC toward an autonomic fate requiring vascular endothelial cell (EC)-secreted nitric oxide (NO) and direct contact with vascular smooth muscle cells (VSMCs) via T-cadherin-mediated homotypic interactions. Once a neurovascular template has been established, NT-derived central neurons then align themselves with the vasculature. Our findings reveal that, in early human development, the autonomic nervous system forms in response to distinct molecular cues from VSMCs and ECs, providing a model for how other developing lineages might coordinate their co-patterning.

### Scientific Abstract:

To gain insight into the cellular and molecular cues that promote neurovascular co-patterning at the earliest stages of human embryogenesis, we developed a human embryonic stem cell model to mimic the developing epiblast. Contact of ectoderm-derived neural cells with mesoderm-derived vasculature is initiated via the neural crest (NC), not the neural tube (NT). Neurovascular co-patterning then ensues with specification of NC toward an autonomic fate requiring vascular endothelial cell (EC)-secreted nitric oxide (NO) and direct contact with vascular smooth muscle cells (VSMCs) via T-cadherin-mediated homotypic interactions. Once a neurovascular template has been established, NT-derived central neurons then align themselves with the vasculature. Our findings reveal that, in early human development, the autonomic nervous system forms in response to distinct molecular cues from VSMCs and ECs, providing a model for how other developing lineages might coordinate their co-patterning.

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